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     (FILE 'HOME' ENTERED AT 10:23:14 ON 19 NOV 2007)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 10:23:43 ON 19 NOV 2007
L1          3366 S "MAPKAP KINASE 2" OR MK2
L2             6 S SHC AND L1
L3             3 DUP REM L2 (3 DUPLICATES REMOVED)
L4             1 S L1 AND (YEAST (3W)ASSAY)
L5           919 S L1 AND (MODULATOR? OR INHIBITOR? OR ACTIVATOR?)
L6             1 S L5 AND (HYBRID ASSAY)
               E YONNANI Y M/AU
               E YANNONI Y/AU
L7            48 S E3-E6
               E LIN L L/AU
L8           526 S E3
L9           570 S L7 OR L8
L10           23 S L1 AND L9
L11            7 DUP REM L10 (16 DUPLICATES REMOVED)
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NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	JUL 02	LMEDLINE coverage updated
NEWS	3	JUL 02	SCISEARCH enhanced with complete author names
NEWS	4	JUL 02	CHEMCATS accession numbers revised
NEWS	5	JUL 02	CA/CAplus enhanced with utility model patents from China
NEWS	6	JUL 16	CAplus enhanced with French and German abstracts
NEWS	7	JUL 18	CA/CAplus patent coverage enhanced
NEWS	8	JUL 26	USPATFULL/USPAT2 enhanced with IPC reclassification
NEWS	9	JUL 30	USGENE now available on STN
NEWS	10	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS	11	AUG 06	FSTA enhanced with new thesaurus edition
NEWS	12	AUG 13	CA/CAplus enhanced with additional kind codes for granted patents
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NEWS	14	AUG 27	Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS	15	AUG 27	USPATOLD now available on STN
NEWS	16	AUG 28	CAS REGISTRY enhanced with additional experimental spectral property data
NEWS	17	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS	18	SEP 13	FORIS renamed to SOFIS
NEWS	19	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS	20	SEP 17	CA/CAplus enhanced with printed CA page images from 1967-1998
NEWS	21	SEP 17	CAplus coverage extended to include traditional medicine patents
NEWS	22	SEP 24	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS	23	OCT 02	CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt
NEWS	24	OCT 19	BEILSTEIN updated with new compounds
NEWS	25	NOV 15	Derwent Indian patent publication number format enhanced
NEWS	26	NOV 19	WPIX enhanced with XML display format

NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

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FILE 'HOME' ENTERED AT 10:23:14 ON 19 NOV 2007

=> file medline embase biosis biotechds scisearch hcaplus ntis lifesci
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 0.21 0.21

FILE 'MEDLINE' ENTERED AT 10:23:43 ON 19 NOV 2007

FILE 'EMBASE' ENTERED AT 10:23:43 ON 19 NOV 2007
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FILE 'LIFESCI' ENTERED AT 10:23:43 ON 19 NOV 2007
COPYRIGHT (C) 2007 Cambridge Scientific Abstracts (CSA)

=> s "MAPKAP kinase 2" or MK2
L1 3366 "MAPKAP KINASE 2" OR MK2

=> s Shc and l1
L2 6 SHC AND L1

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3 3 DUP REM L2 (3 DUPLICATES REMOVED)

=> d 1-3 ibib ab

L3 ANSWER 1 OF 3 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
DUPLICATE 1
ACCESSION NUMBER: 2004-09118 BIOTECHDS
TITLE: New isolated, purified or recombinant protein complex comprising an MK2 polypeptide, and an MK2 interacting protein chosen from STS, HPH2 and Shc for treating or preventing e.g. Crohn's disease, or rheumatoid arthritis;
involving vector-mediated gene transfer and expression in host cell for use in gene therapy
AUTHOR: LIN L; YANNONI Y M
PATENT ASSIGNEE: WYETH

PATENT INFO: WO 2004012660 12 Feb 2004
APPLICATION INFO: WO 2003-US23981 1 Aug 2003
PRIORITY INFO: US 2002-400044 2 Aug 2002; US 2002-400044 2 Aug 2002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2004-156998 [15]

AB DERWENT ABSTRACT:

NOVELTY - An isolated, purified or recombinant protein complex comprising a mitogen-activated protein kinase-activated protein kinase 2 (MK2) polypeptide, and an MK2 interacting protein chosen from STS, HPH2 and Shc, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following: (1) a host cell comprising a first and a second nucleic acid, where the first nucleic acid encodes a recombinant MK2 polypeptide and the second nucleic acid encoding MK2 interacting protein; (2) an assay for determining whether the test compound inhibits or promotes formation of a protein complex; (3) a method for determining whether a test compound affects MK2 activity; (4) an screening assay to identify compounds that inhibit or promote formation of the protein complex; (5) an antibody that binds one or more proteins in the complex; (6) a method for modulating formation of a protein complex in a cell comprising at least a first and a second protein; (7) a method for producing a complex; (8) a drug screening method for identifying anti-inflammatory drugs; (9) a method of modulating inflammation in a tissue; (10) a method of treating or preventing inflammation in a tissue; (11) a method of treating a patient suffering from at least one inflammatory condition; (12) a method of expressing a nucleic acid in a cell to inhibit inflammation; (13) a method of detecting at least one of the absence, presence and amount of MK2 in a sample; (14) a kit that enables qualitative detection of MK2 comprising a compound that interacts with at least one of MK2 or an MK2 complex, where the compound is chosen from an antibody, a chemical agent, a small molecule, a protein and a peptide; and at least one other kit component chosen from: at least one of buffer and solution; and at least one structural component; and (15) a pharmaceutical composition comprising at least one protein that binds MK2, and at least one carrier.

BIOTECHNOLOGY - Preferred Complex: The protein complex comprises an MK2 polypeptide and at least one or two MK2 interacting protein. The MK2 interacting protein is chosen from STS, HPH2 and Shc. The MK2 polypeptide comprises a fusion protein. The fusion protein comprises a domain for purifying, isolating or detecting the fusion protein. The fusion protein comprises a domain chosen from affinity tags, radionucleotides, enzymes, and fluorophores. The domain is selected from polyhistidine, FLAG, Glu-Glu, glutathione S transferase (GST), thioredoxin, protein A, protein G, and an immunoglobulin heavy chain constant region. Preferred Method: Determining whether a test compound inhibits or promotes formation of a protein complex comprises forming a reaction mixture including an MK2 polypeptide, at least one MK2 interacting protein and the test compound; and detecting the presence of the protein complex between MK2 and the MK2 interacting protein, where a difference in the amount of complex in the presence of the test compound, relative to the amount of complex in the absence of the test compound indicates that the test compound inhibits or promotes complex formation. An increase in the amount of complex in presence of the test compound indicates that the test compound promotes complex formation. A decrease in the amount of complex in presence of the test compound indicates that the test compound inhibits complex formation. Determining whether a test compound affects MK2 activity comprises forming a protein complex comprising an MK2 polypeptide and an MK2 interacting protein; contacting the protein complex with the test compound; and determining the effect of the test compound on one or more activities chosen from MK2 kinase activity, an amount of

MK2 in the complex, production of TNF, and amount of phosphorylated form of a substrate of MK2. The screening assay to identify compounds that inhibit or promote formation of a protein complex, comprises providing a two-hybrid assay system including a first fusion protein comprising an MK2 polypeptide, and a second fusion protein comprising a polypeptide chosen from one or more of STS, HPH2 and Shc, under conditions where the two proteins interact in the two hybrid assay system; measuring a level of interaction between the fusion proteins in the presence and in the absence of a test compound; and comparing the level of interaction of the fusion proteins, where a decrease in the level of interaction is indicative of a compound that inhibits the interaction between the MK2 polypeptide and a polypeptide chosen from one or more of STS, HPH2 and Shc. Modulating formation of a protein complex in a cell comprising at least a first protein and a second protein, where the first protein is an MK2 polypeptide and the second protein is chosen from one or more of STS, HPH2 and Shc, comprises administering to the cell a compound capable of modulating formation of the complex. Producing a complex comprises transfecting a cell with one or more polynucleotides encoding an MK2 polypeptide and an MK2 interacting protein chosen from one or more of STS and Shc, where the polypeptides form a complex. The drug screening method for identifying anti-inflammatory drugs comprises providing MK2 and at least one MK2-interacting protein; allowing MK2 and the protein to interact to form a complex; adding an effective amount of a potential drug to the complex; and determining whether the potential drug inhibits complex formation. The MK2 and the protein interact in vivo in a yeast or mammalian 2-hybrid system. The MK2 and the protein interact in vitro. The protein is STS, Shc or HPH2. The drug is a small molecule, peptide or protein, antibody, or chemical agent. Modulating inflammation in a tissue comprises administering a nucleic acid that encodes an MK2 interacting protein to the tissue; and allowing the nucleic acid to express the MK2 interacting protein, thus to modulate inflammation in the tissue. The nucleic acid expresses a protein chosen from STS, HPH2 and Shc. Treating or preventing inflammation in a tissue comprises administering to the tissue a therapeutically effective amount of at least one agent that blocks the interaction between MK2 and an MK2 interacting protein; or allows the interaction, but blocks MK2 activity. The agent is an antibody, preferably a polyclonal or monoclonal antibody. The antibody binds MK2 or the MK2 -interacting protein. The agent is a chemical agent, a peptide or protein, or a small molecule. Modulating inflammation in a tissue comprises contacting the tissue with at least one protein that binds MK2; and allowing the protein to modulate inflammation in the tissue. Treating a patient suffering from at least one inflammatory condition, comprises administering a therapeutically effective dose of at least one compound chosen from a compound that interacts with at least one of MK2 or an MK2 complex, where the compound is chosen from an antibody, a chemical agent, a small molecule, a protein and a peptide; and allowing the compound to bind to at least one of MK2 or an MK2 complex and modulate inflammation. The protein or peptide is a mutant form of a wild-type protein or peptide, which stimulates MK2 activity. Expressing a nucleic acid in a cell to inhibit inflammation comprises adding at least one nucleic acid encoding a compound chosen from a compound that interacts with at least one of MK2 or an MK2 complex, where the compound is chosen from an antibody, a chemical agent, a small molecule, a protein and a peptide; and allowing the cell to express the compound and inhibit inflammation. Detecting at least one of the absence, presence, and amount of MK2 in a sample, comprises administering at least one compound that interacts with at least one of MK2 or an MK2 complex, where the compound is chosen from an antibody, a chemical agent, a small molecule, a protein and a peptide; and

correlating the absence, presence, or amount of bound protein or compound with the absence, presence, or amount of MK2 in the sample. Preferred Antibody: The antibody inhibits interaction of MK2 with the MK2 interacting protein. Preferred Kit: The kit further comprises an agent that binds the protein or compound. The agent is an antibody.

ACTIVITY - Antiinflammatory; Gastrointestinal; Antiarthritic; Antirheumatic; Respiratory-Gen; Antiasthmatic; Immunosuppressive; Antiulcer. No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The composition and methods are useful for treating or preventing a condition chosen from Crohn's disease, inflammatory bowel disease, ulcerative colitis, rheumatoid arthritis, acute respiratory distress syndrome, emphysema, delayed type hypersensitivity reaction, asthma, systemic lupus erythematosus, and inflammation due to trauma or injury (claimed).

ADMINISTRATION - Dosage is 5-500, preferably 40-60 mg per kg. Administration is intravenous, intramuscular, rectal or subcutaneous.

EXAMPLE - Experimental protocols are described but no results are given. (107 pages)

L3 ANSWER 2 OF 3 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2004196650 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15094067
TITLE: P66(ShcA) interacts with MAPKAP kinase 2 and regulates its activity.
AUTHOR: Yannoni Yvonne M; Gaestel Matthias; Lin Lih-Ling
CORPORATE SOURCE: Department of Inflammation, Wyeth Research, 200 Cambridge Park Drive, Cambridge, MA 02140-2311, USA.. yvonne.yannoni@abbott.com
SOURCE: FEBS letters, (2004 Apr 23) Vol. 564, No. 1-2, pp. 205-11. Journal code: 0155157. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 20 Apr 2004
Last Updated on STN: 4 Jun 2004
Entered Medline: 3 Jun 2004

AB Three mitogen activated protein kinase-activated protein kinase 2 (MAPKAP kinase 2, MK2) interacting proteins were identified using a yeast two-hybrid approach. ShcA, a signaling phospho-protein, human polyhomeotic 2 (HPH2), a transcriptional regulator, and highly similar to smoothelin (HSTS), which is related to the cytoskeletal associated protein smoothelin, interact specifically with MK2. The interaction of MK2 with the 66 kDa isoform of ShcA, p66(ShcA), and HPH2 was confirmed using co-immunoprecipitation. MK2 is activated with p66(ShcA) co-expression and p66(ShcA) is an in vitro substrate for MK2, further demonstrating their association and suggesting a biological role for p66(Shc) in MK2 activation.

L3 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:615889 HCAPLUS
DOCUMENT NUMBER: 137:180730
TITLE: Human cDNA/DNA molecules and proteins encoded by them with enhanced expression in apoptosis-resistant cell clones, and use thereof in diagnosis, therapeutics and drug screening
INVENTOR(S): Ullrich, Axel; Abraham, Reimar
PATENT ASSIGNEE(S): Max-Planck-Gesellschaft zur Foerderung der Wissenschaften e.V., Germany
SOURCE: PCT Int. Appl., 56 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002063037	A2	20020815	WO 2002-EP1073	20020201
WO 2002063037	A3	20031002		
WO 2002063037	A9	20040219		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2434881	A1	20020815	CA 2002-2434881	20020201
AU 2002249170	A1	20020819	AU 2002-249170	20020201
AU 2002249170	B2	20070208		
EP 1364066	A2	20031126	EP 2002-718083	20020201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004517638	T	20040617	JP 2002-562773	20020201
US 2004110177	A1	20040610	US 2003-470845	20030731
AU 2007201963	A1	20070524	AU 2007-201963	20070502
PRIORITY APPLN. INFO.:			US 2001-265631P P	20010202
			AU 2002-249170 A3	20020201
			WO 2002-EP1073 W	20020201

AB The present invention relates to a method for identifying nucleic acid mols. functionally associated with a desired phenotype, such as cancer cell properties, including anti-apoptosis. The method, which allows for generation of expression profiles of genes associated with said desired phenotype, involves a mutagenesis and/or genome rearrangement step, followed by selection of cell clones displaying the desired phenotype. The invention also relates that the method involves the use of the following techniques: fluorescence-activated cell sorting (FACS); nucleic acid microarray (cDNA, genomic or oligonucleotide); protein array; two-dimensional gel electrophoresis; and/or mass spectrometry. The invention further relates that the disclosed method was used to identify genes, which are differentially expressed in apoptosis-sensitive and apoptosis-resistant cells. Specifically, the invention relates that apoptosis was induced in human cervix carcinoma cell line HeLa S3 by Fas activation. After the selection procedure, only a low number of living cells were present, which had a higher resistance against apoptosis than the parental cell line. MRNA was isolated from these surviving clones, and from the parental cell line, and transcribed into cDNA. CDNA microarray technol. was used to identify about 150-200 genes (cDNA/DNA mols.) that exhibited enhanced expression in apoptosis-resistant clones. The GenBank accession nos. of some of these cDNA/DNA mols. are provided, along with the products encoded by said mols. Still further, the invention relates that most of the apoptosis-associated genes encode protein phosphatases, and kinases. Finally, the invention relates that said nucleic acid mols., and proteins encoded by mols., can be used as targets in diagnosis, therapeutics and drug screening, particularly for disorders associated with dysfunction of apoptotic processes, such as tumors.

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     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 10:23:43 ON 19 NOV 2007
L1          3366 S "MAPKAP KINASE 2" OR MK2
L2             6 S SHC AND L1
L3             3 DUP REM L2 (3 DUPLICATES REMOVED)

=> s l1 and (yeast (3w)assay)
L4             1 L1 AND (YEAST (3W) ASSAY)

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L4   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2001:417251  HCAPLUS
DOCUMENT NUMBER:          135:30736
TITLE:                    Protein-protein interactions involving human kinases
                          and their uses in disease diagnosis and drug screening
INVENTOR(S):              Heichman, Karen; Cimbora, Daniel M.; Bush, Angie;
                          Mauck, Kimberly; Bartel, Paul L.
PATENT ASSIGNEE(S):       Myriad Genetics, Inc., USA
SOURCE:                   PCT Int. Appl., 97 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   19
PATENT INFORMATION:

     PATENT NO.            KIND   DATE        APPLICATION NO.          DATE
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     WO 2001040794          A1    20010607    WO 2000-US32619          20001201
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             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
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             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,
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     CA 2396460             A1    20010607    CA 2000-2396460          20001201
     EP 1234174             A1    20020828    EP 2000-982312           20001201
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PRIORITY APPLN. INFO.:                       US 1999-168377P      P  19991202
                                             US 1999-168379P      P  19991202
                                             US 2000-185056P      P  20000225
                                             WO 2000-US32619      W  20001201
AB   The present invention relates to the discovery of novel protein-protein
     interactions that are involved in mammalian physiol. pathways, including
     physiol. disorders or diseases.  Examples of physiol. disorders and
     diseases include non-insulin dependent diabetes mellitus,
     neurodegenerative disorders, such as Alzheimer's Disease, and the like.
     Thus, the present invention is directed to complexes of these proteins
     and/or their fragments, antibodies to the complexes, diagnosis of physiol.
     generative disorders (including diagnosis of a predisposition to and
     diagnosis of the existence of the disorder), drug screening for agents
     which modulate the interaction of proteins described herein, and
     identification of addnl. proteins in the pathway common to the proteins
     described herein.  The yeast two-hybrid assay
     identified interactions of human p38α kinase, MAP kinase activators
     3pK and 2pK, PRAK kinase, and MSK-1 kinase with various protein
     modulators.
REFERENCE COUNT:          5      THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
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     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 10:23:43 ON 19 NOV 2007
L1          3366 S "MAPKAP KINASE 2" OR MK2
L2             6 S SHC AND L1
L3             3 DUP REM L2 (3 DUPLICATES REMOVED)
L4             1 S L1 AND (YEAST (3W)ASSAY)

=> s l1 and (modulator? or inhibitor? or activator?)
L5          919 L1 AND (MODULATOR? OR INHIBITOR? OR ACTIVATOR?)

=> s l5 and (hybrid assay)
L6            1 L5 AND (HYBRID ASSAY)

=> d ibib ab

L6   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2001:417251  HCAPLUS
DOCUMENT NUMBER:          135:30736
TITLE:                    Protein-protein interactions involving human kinases
                          and their uses in disease diagnosis and drug screening
INVENTOR(S):              Heichman, Karen; Cimbora, Daniel M.; Bush, Angie;
                          Mauck, Kimberly; Bartel, Paul L.
PATENT ASSIGNEE(S):       Myriad Genetics, Inc., USA
SOURCE:                   PCT Int. Appl., 97 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   19
PATENT INFORMATION:

     PATENT NO.            KIND   DATE        APPLICATION NO.          DATE
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     WO 2001040794          A1    20010607    WO 2000-US32619          20001201
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             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
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             ZA, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
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     EP 1234174             A1    20020828    EP 2000-982312           20001201
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRIORITY APPLN. INFO.:                       US 1999-168377P     P  19991202
                                             US 1999-168379P     P  19991202
                                             US 2000-185056P     P  20000225
                                             WO 2000-US32619     W  20001201
AB   The present invention relates to the discovery of novel protein-protein
     interactions that are involved in mammalian physiol. pathways, including
     physiol. disorders or diseases.  Examples of physiol. disorders and
     diseases include non-insulin dependent diabetes mellitus,
     neurodegenerative disorders, such as Alzheimer's Disease, and the like.
     Thus, the present invention is directed to complexes of these proteins
     and/or their fragments, antibodies to the complexes, diagnosis of physiol.
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generative disorders (including diagnosis of a predisposition to and diagnosis of the existence of the disorder), drug screening for agents which modulate the interaction of proteins described herein, and identification of addnl. proteins in the pathway common to the proteins described herein. The yeast two-hybrid assay identified interactions of human p38α kinase, MAP kinase activators 3pK and 2pK, PRAK kinase, and MSK-1 kinase with various protein modulators.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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E5           17     YONNEAU LAURENT/AU
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E7            1     YONNER PIERRE/AU
E8            1     YONNET C/AU
E9            1     YONNET CATHERINE/AU
E10          13     YONNET G/AU
E11           1     YONNET GINETTE/AU
E12         128     YONNET J/AU

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E7            1     YANNONL COSTANTINO S/AU
E8            1     YANNONNI C S/AU
E9           43     YANNOPAPAS V/AU
E10          18     YANNOPAPAS VASSILIOS/AU
E11           1     YANNOPAPAS VASSILIS/AU
E12           1     YANNOPOLOS J C/AU

=> s e3-e6
L7           48 ("YANNONI Y"/AU OR "YANNONI Y M"/AU OR "YANNONI YVONNE"/AU OR
                "YANNONI YVONNE M"/AU)

=> e lin l l/au
E1          132     LIN L K/AU
E2            1     LIN L KH/AU
E3          526 --> LIN L L/AU
E4            1     LIN L L J/AU
E5          171     LIN L L K/AU
E6            2     LIN L L L/AU
E7            1     LIN L L Y/AU
E8          380     LIN L M/AU
E9            1     LIN L M P/AU
E10           1     LIN L MICHAEL/AU
E11         140     LIN L N/AU
E12         196     LIN L P/AU

=> s e3
L8          526 "LIN L L"/AU

=> d his

     (FILE 'HOME' ENTERED AT 10:23:14 ON 19 NOV 2007)
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     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 10:23:43 ON 19 NOV 2007
L1          3366 S "MAPKAP KINASE 2" OR MK2
L2             6 S SHC AND L1
L3             3 DUP REM L2 (3 DUPLICATES REMOVED)
L4             1 S L1 AND (YEAST (3W)ASSAY)
L5           919 S L1 AND (MODULATOR? OR INHIBITOR? OR ACTIVATOR?)
L6             1 S L5 AND (HYBRID ASSAY)
               E YONNANI Y M/AU
               E YANNONI Y/AU
L7            48 S E3-E6
               E LIN L L/AU
L8           526 S E3

=> s l7 or l8
L9          570 L7 OR L8

=> s l1 and l9
L10          23 L1 AND L9

=> dup rem l10
PROCESSING COMPLETED FOR L10
L11           7 DUP REM L10 (16 DUPLICATES REMOVED)

=> d 1-7 ibib ab

L11  ANSWER 1 OF 7  EMBASE  COPYRIGHT (c) 2007 Elsevier B.V. All rights
     reserved on STN
ACCESSION NUMBER:    2007385192  EMBASE
TITLE:               Identification of a novel class of selective Tpl2 kinase
                     inhibitors: 4-Alkylamino-[1,7]naphthyridine-3-
                     carbonitriles.
AUTHOR:              Kaila N.; Green N.; Li H.-Q.; Hu Y.; Janz K.; Gavrin L.K.;
                     Thomason J.; Tam S.; Powell D.; Cuozzo J.; Hall J.P.;
                     Telliez J.-B.; Hsu S.; Nickerson-Nutter C.; Wang Q.;
                     Lin L.-L.
CORPORATE SOURCE:    N. Kaila, Chemical and Screening Sciences (CSS), Wyeth
                     Research, 200 CambridgePark Drive, Cambridge, MA 02140,
                     United States. nkaila@wyeth.com
SOURCE:              Bioorganic and Medicinal Chemistry, (1 Oct 2007) Vol. 15,
                     No. 19, pp. 6425-6442.
                     Refs: 35
                     ISSN: 0968-0896  CODEN: BMECEP
PUBLISHER IDENT.:    S 0968-0896(07)00590-1
COUNTRY:             United Kingdom
DOCUMENT TYPE:       Journal; Article
FILE SEGMENT:        016     Cancer
                     037     Drug Literature Index
LANGUAGE:            English
SUMMARY LANGUAGE:    English
ENTRY DATE:          Entered STN: 6 Sep 2007
                     Last Updated on STN: 6 Sep 2007
AB   We have previously reported the discovery and initial SAR of the
     [1,7]naphthyridine-3-carbonitriles and quinoline-3-carbonitriles as Tumor
     Progression Loci-2 (Tpl2) kinase inhibitors.  In this paper, we report new
     SAR efforts which have led to the identification of 4-alkylamino-
     [1,7]naphthyridine-3-carbonitriles.  These compounds show good in vitro
     and in vivo activity against Tpl2 and improved pharmacokinetic properties.
     In addition they are highly selective for Tpl2 kinase over other kinases,
     for example, EGFR, MEK, MK2, and p38.  Lead compound
     4-cycloheptylamino-6-[(pyridin-3-ylmethyl)-amino]-[1,7]naphthyridine-3-
     carbonitrile (30) was efficacious in a rat model of LPS-induced
     TNF-α production. .COPYRGT. 2007 Elsevier Ltd.  All rights reserved.
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L11 ANSWER 2 OF 7 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2006728868 MEDLINE
DOCUMENT NUMBER: PubMed ID: 17030606
TITLE: The mitogen-activated protein kinase (MAPK)-activated protein kinases MK2 and MK3 cooperate in stimulation of tumor necrosis factor biosynthesis and stabilization of p38 MAPK.
AUTHOR: Ronkina N; Kotlyarov A; Dittrich-Breiholz O; Kracht M; Hitti E; Milarski K; Askew R; Marusic S; Lin L-L; Gaestel M; Telliez J-B
CORPORATE SOURCE: Institute of Biochemistry, Medical School Hannover, Carl-Neuberg-Strasse 1, D-30625 Hannover, Germany.
SOURCE: Molecular and cellular biology, (2007 Jan) Vol. 27, No. 1, pp. 170-81. Electronic Publication: 2006-10-09. Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200701
ENTRY DATE: Entered STN: 15 Dec 2006
Last Updated on STN: 19 Jan 2007
Entered Medline: 18 Jan 2007

AB MK2 and MK3 represent protein kinases downstream of p38 mitogen-activated protein kinase (MAPK). Deletion of the MK2 gene in mice resulted in an impaired inflammatory response although MK3, which displays extensive structural similarities and identical functional properties in vitro, is still present. Here, we analyze tumor necrosis factor (TNF) production and expression of p38 MAPK and tristetraprolin (TTP) in MK3-deficient mice and demonstrate that there are no significant differences with wild-type animals. We show that in vivo MK2 and MK3 are expressed and activated in parallel. However, the level of activity of MK2 is always significantly higher than that of MK3. Accordingly, we hypothesized that MK3 could have significant effects only in an MK2-free background and generated MK2/MK3 double-knockout mice. Unexpectedly, these mice are viable and show no obvious defects due to loss of compensation between MK2 and MK3. However, there is a further reduction of TNF production and expression of p38 and TTP in double-knockout mice compared to MK2-deficient mice. This finding, together with the observation that ectopically expressed MK3 can rescue MK2 deficiency similarly to MK2 , indicates that both kinases share the same physiological function in vivo but are expressed to different levels.

L11 ANSWER 3 OF 7 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN DUPLICATE 2
ACCESSION NUMBER: 2006348501 EMBASE
TITLE: MAPKAP kinase 2-deficient mice are resistant to collagen-induced arthritis.
AUTHOR: Hegen M.; Gaestel M.; Nickerson-Nutter C.L.; Lin L.-L.; Telliez J.-B.
CORPORATE SOURCE: Dr. M. Hegen, Wyeth Research, 200 Cambridge Park Drive, Cambridge, MA 02140, United States. Mhegen@wyeth.com
SOURCE: Journal of Immunology, (1 Aug 2006) Vol. 177, No. 3, pp. 1913-1917.
Refs: 21
ISSN: 0022-1767 CODEN: JOIMA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
LANGUAGE: English

SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 11 Aug 2006
Last Updated on STN: 11 Aug 2006

AB TNF-α is a pleiotropic cytokine considered a primary mediator of immune regulation and inflammatory response and has been shown to play a central role in rheumatoid arthritis (RA). MAPKAP kinase 2 (MK2) is a serine/threonine kinase that is regulated through direct phosphorylation by p38 MAPK, and has been shown to be an essential component in the inflammatory response that regulates the biosynthesis of TNF-α at a posttranscriptional level. The murine model of collagen-induced arthritis (CIA) is an established disease model to study pathogenic mechanisms relevant to RA. In this study, we report that deletion of the MK2 gene in DBA/1LacJ mice confers protection against CIA. Interestingly, the MK2 heterozygous mutants display an intermediate level of protection when compared with homozygous mutant and wild-type littermates. We show that MK2(-/-) and MK2(+/-) mice exhibit decreased disease incidence and severity in the CIA disease model and reduced TNF-α and IL-6 serum levels following LPS/D-Gal treatment compared with wild-type mice. Additionally, we show that levels of IL-6 mRNA in paws of mice with CIA correlate with the disease status. These findings suggest that an MK2 inhibitor could be of great therapeutic value to treat inflammatory diseases like RA. Copyright .COPYRGT. 2006 by The American Association of Immunologists, Inc.

L11 ANSWER 4 OF 7 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
DUPLICATE 3
ACCESSION NUMBER: 2004-09118 BIOTECHDS
TITLE: New isolated, purified or recombinant protein complex comprising an MK2 polypeptide, and an MK2 interacting protein chosen from STS, HPH2 and Shc for treating or preventing e.g. Crohn's disease, or rheumatoid arthritis;
involving vector-mediated gene transfer and expression in host cell for use in gene therapy
AUTHOR: LIN L; YANNONI Y M
PATENT ASSIGNEE: WYETH
PATENT INFO: WO 2004012660 12 Feb 2004
APPLICATION INFO: WO 2003-US23981 1 Aug 2003
PRIORITY INFO: US 2002-400044 2 Aug 2002; US 2002-400044 2 Aug 2002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2004-156998 [15]

AB DERWENT ABSTRACT:
NOVELTY - An isolated, purified or recombinant protein complex comprising a mitogen-activated protein kinase-activated protein kinase 2 (MK2) polypeptide, and an MK2 interacting protein chosen from STS, HPH2 and Shc, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following: (1) a host cell comprising a first and a second nucleic acid, where the first nucleic acid encodes a recombinant MK2 polypeptide and the second nucleic acid encoding MK2 interacting protein; (2) an assay for determining whether the test compound inhibits or promotes formation of a protein complex; (3) a method for determining whether a test compound affects MK2 activity; (4) an screening assay to identify compounds that inhibit or promote formation of the protein complex; (5) an antibody that binds one or more proteins in the complex; (6) a method for modulating formation of a protein complex in a cell comprising at least a first and a second protein; (7) a method for producing a complex; (8) a drug screening method for identifying anti-inflammatory drugs; (9) a method of modulating inflammation in a tissue; (10) a method of treating or preventing inflammation in a tissue; (11) a method of treating a patient suffering from at least one inflammatory condition; (12) a method of

expressing a nucleic acid in a cell to inhibit inflammation; (13) a method of detecting at least one of the absence, presence and amount of MK2 in a sample; (14) a kit that enables qualitative detection of MK2 comprising a compound that interacts with at least one of MK2 or an MK2 complex, where the compound is chosen from an antibody, a chemical agent, a small molecule, a protein and a peptide; and at least one other kit component chosen from: at least one of buffer and solution; and at least one structural component; and (15) a pharmaceutical composition comprising at least one protein that binds MK2, and at least one carrier.

BIOTECHNOLOGY - Preferred Complex: The protein complex comprises an MK2 polypeptide and at least one or two MK2 interacting protein. The MK2 interacting protein is chosen from STS, HPH2 and Shc. The MK2 polypeptide comprises a fusion protein. The fusion protein comprises a domain for purifying, isolating or detecting the fusion protein. The fusion protein comprises a domain chosen from affinity tags, radionucleotides, enzymes, and fluorophores. The domain is selected from polyhistidine, FLAG, Glu-Glu, glutathione S transferase (GST), thioredoxin, protein A, protein G, and an immunoglobulin heavy chain constant region. Preferred Method: Determining whether a test compound inhibits or promotes formation of a protein complex comprises forming a reaction mixture including an MK2 polypeptide, at least one MK2 interacting protein and the test compound; and detecting the presence of the protein complex between MK2 and the MK2 interacting protein, where a difference in the amount of complex in the presence of the test compound, relative to the amount of complex in the absence of the test compound indicates that the test compound inhibits or promotes complex formation. An increase in the amount of complex in presence of the test compound indicates that the test compound promotes complex formation. A decrease in the amount of complex in presence of the test compound indicates that the test compound inhibits complex formation. Determining whether a test compound affects MK2 activity comprises forming a protein complex comprising an MK2 polypeptide and an MK2 interacting protein; contacting the protein complex with the test compound; and determining the effect of the test compound on one or more activities chosen from MK2 kinase activity, an amount of MK2 in the complex, production of TNF, and amount of phosphorylated form of a substrate of MK2. The screening assay to identify compounds that inhibit or promote formation of a protein complex, comprises providing a two-hybrid assay system including a first fusion protein comprising an MK2 polypeptide, and a second fusion protein comprising a polypeptide chosen from one or more of STS, HPH2 and Shc, under conditions where the two proteins interact in the two hybrid assay system; measuring a level of interaction between the fusion proteins in the presence and in the absence of a test compound; and comparing the level of interaction of the fusion proteins, where a decrease in the level of interaction is indicative of a compound that inhibits the interaction between the MK2 polypeptide and a polypeptide chosen from one or more of STS, HPH2 and Shc. Modulating formation of a protein complex in a cell comprising at least a first protein and a second protein, where the first protein is an MK2 polypeptide and the second protein is chosen from one or more of STS, HPH2 and Shc, comprises administering to the cell a compound capable of modulating formation of the complex. Producing a complex comprises transfecting a cell with one or more polynucleotides encoding an MK2 polypeptide and an MK2 interacting protein chosen from one or more of STS and Shc, where the polypeptides form a complex. The drug screening method for identifying anti-inflammatory drugs comprises providing MK2 and at least one MK2-interacting protein; allowing MK2 and the protein to interact to form a complex; adding an effective amount of a potential drug to the complex; and determining whether the potential drug inhibits complex formation. The MK2 and the protein interact in vivo in a yeast or mammalian 2-hybrid system. The MK2 and the

protein interact in vitro. The protein is STS, Shc or HPH2. The drug is a small molecule, peptide or protein, antibody, or chemical agent. Modulating inflammation in a tissue comprises administering a nucleic acid that encodes an MK2 interacting protein to the tissue; and allowing the nucleic acid to express the MK2 interacting protein, thus to modulate inflammation in the tissue. The nucleic acid expresses a protein chosen from STS, HPH2 and Shc. Treating or preventing inflammation in a tissue comprises administering to the tissue a therapeutically effective amount of at least one agent that blocks the interaction between MK2 and an MK2 interacting protein; or allows the interaction, but blocks MK2 activity. The agent is an antibody, preferably a polyclonal or monoclonal antibody. The antibody binds MK2 or the MK2-interacting protein. The agent is a chemical agent, a peptide or protein, or a small molecule. Modulating inflammation in a tissue comprises contacting the tissue with at least one protein that binds MK2; and allowing the protein to modulate inflammation in the tissue. Treating a patient suffering from at least one inflammatory condition, comprises administering a therapeutically effective dose of at least one compound chosen from a compound that interacts with at least one of MK2 or an MK2 complex, where the compound is chosen from an antibody, a chemical agent, a small molecule, a protein and a peptide; and allowing the compound to bind to at least one of MK2 or an MK2 complex and modulate inflammation. The protein or peptide is a mutant form of a wild-type protein or peptide, which stimulates MK2 activity. Expressing a nucleic acid in a cell to inhibit inflammation comprises adding at least one nucleic acid encoding a compound chosen from a compound that interacts with at least one of MK2 or an MK2 complex, where the compound is chosen from an antibody, a chemical agent, a small molecule, a protein and a peptide; and allowing the cell to express the compound and inhibit inflammation. Detecting at least one of the absence, presence, and amount of MK2 in a sample, comprises administering at least one compound that interacts with at least one of MK2 or an MK2 complex, where the compound is chosen from an antibody, a chemical agent, a small molecule, a protein and a peptide; and correlating the absence, presence, or amount of bound protein or compound with the absence, presence, or amount of MK2 in the sample. Preferred Antibody: The antibody inhibits interaction of MK2 with the MK2 interacting protein. Preferred Kit: The kit further comprises an agent that binds the protein or compound. The agent is an antibody.

ACTIVITY - Antiinflammatory; Gastrointestinal; Antiarthritic; Antirheumatic; Respiratory-Gen; Antiasthmatic; Immunosuppressive; Antiulcer. No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The composition and methods are useful for treating or preventing a condition chosen from Crohn's disease, inflammatory bowel disease, ulcerative colitis, rheumatoid arthritis, acute respiratory distress syndrome, emphysema, delayed type hypersensitivity reaction, asthma, systemic lupus erythematosus, and inflammation due to trauma or injury (claimed).

ADMINISTRATION - Dosage is 5-500, preferably 40-60 mg per kg. Administration is intravenous, intramuscular, rectal or subcutaneous.

EXAMPLE - Experimental protocols are described but no results are given. (107 pages)

L11 ANSWER 5 OF 7 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2004196650 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15094067
TITLE: P66(ShcA) interacts with MAPKAP kinase 2 and regulates its activity.
AUTHOR: Yannoni Yvonne M; Gaestel Matthias; Lin Lih-Ling
CORPORATE SOURCE: Department of Inflammation, Wyeth Research, 200 Cambridge

Park Drive, Cambridge, MA 02140-2311, USA..
yvonne.yannoni@abbott.com
SOURCE: FEBS letters, (2004 Apr 23) Vol. 564, No. 1-2, pp. 205-11.
Journal code: 0155157. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 20 Apr 2004
Last Updated on STN: 4 Jun 2004
Entered Medline: 3 Jun 2004

AB Three mitogen activated protein kinase-activated protein kinase 2 (MAPKAP kinase 2, MK2) interacting proteins were identified using a yeast two-hybrid approach. ShcA, a signaling phospho-protein, human polyhomeotic 2 (HPH2), a transcriptional regulator, and highly similar to smoothelin (HSTS), which is related to the cytoskeletal associated protein smoothelin, interact specifically with MK2. The interaction of MK2 with the 66 kDa isoform of ShcA, p66(ShcA), and HPH2 was confirmed using co-immunoprecipitation. MK2 is activated with p66(ShcA) co-expression and p66(ShcA) is an in vitro substrate for MK2, further demonstrating their association and suggesting a biological role for p66(Shc) in MK2 activation.

L11 ANSWER 6 OF 7 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN DUPLICATE 5
ACCESSION NUMBER: 2003421872 EMBASE
TITLE: Catalytically active MAP KAP kinase 2 structures in complex with staurosporine and ADP reveal differences with the autoinhibited enzyme.
AUTHOR: Underwood K.W.; Parris K.D.; Federico E.; Mosyak L.; Czerwinski R.M.; Shane T.; Taylor M.; Svenson K.; Liu Y.; Hsiao C.-L.; Wolfrom S.; Maguire M.; Malakian K.; Telliez J.-B.; Lin L.-L.; Kriz R.W.; Seehra J.; Somers W.S.; Stahl M.L.
CORPORATE SOURCE: K.W. Underwood, Department of Biological Chemistry, Wyeth Research, 87 Cambridge Park Drive, Cambridge, MA 02140, United States. kunderwood@wyeth.com
SOURCE: Structure, (Jun 2003) Vol. 11, No. 6, pp. 627-636.
Refs: 39
ISSN: 0969-2126 CODEN: STRUE6
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical and Experimental Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 6 Nov 2003
Last Updated on STN: 6 Nov 2003

AB MAP KAP kinase 2 (MK2), a Ser/Thr kinase, plays a crucial role in the inflammatory process. We have determined the crystal structures of a catalytically active C-terminal deletion form of human MK2, residues 41-364, in complex with staurosporine at 2.7 A and with ADP at 3.2 A, revealing overall structural similarity with other Ser/Thr kinases. Kinetic analysis reveals that the K(m) for ATP is very similar for MK2 41-364 and p38-activated MK2 41-400. Conversely, the catalytic rate and binding for peptide substrate are dramatically reduced in MK2 41-364. However, phosphorylation of MK2 41-364 by p38 restores the V(max) and K (m) for peptide substrate to values comparable to those seen in p38-activated MK2 41-400, suggesting a mechanism for regulation of enzyme activity.

L11 ANSWER 7 OF 7 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2002310533 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12052889
TITLE: Distinct cellular functions of MK2.
AUTHOR: Kotlyarov Alexey; Yannoni Yvonne; Fritz Susann; Laass Kathrin; Telliez Jean-Baptiste; Pitman Deborah; Lin Lih-Ling; Gaestel Matthias
CORPORATE SOURCE: Institute of Biochemistry, Medical School Hannover, Hannover 30625, Germany.
SOURCE: Molecular and cellular biology, (2002 Jul) Vol. 22, No. 13, pp. 4827-35.
Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200207
ENTRY DATE: Entered STN: 11 Jun 2002
Last Updated on STN: 19 Jul 2002
Entered Medline: 18 Jul 2002

AB Mitogen-activated protein kinase (MAPK)-activated protein kinase 2 (MK2) is activated upon stress by p38 MAPK alpha and -beta, which bind to a basic docking motif in the C terminus of MK2 and which subsequently phosphorylate its regulatory sites. As a result of activation MK2 is exported from the nucleus to the cytoplasm and cotransports active p38 MAPK to this compartment. Here we show that the amount of p38 MAPK is significantly reduced in cells and tissues lacking MK2, indicating a stabilizing effect of MK2 for p38.
Using a murine knockout model, we have previously shown that elimination of MK2 leads to a dramatic reduction of tumor necrosis factor (TNF) production in response to lipopolysaccharide. To further elucidate the role of MK2 in p38 MAPK stabilization and in TNF biosynthesis, we analyzed the ability of two MK2 isoforms and several MK2 mutants to restore both p38 MAPK protein levels and TNF biosynthesis in macrophages. We show that MK2 stabilizes p38 MAPK through its C terminus and that MK2 catalytic activity does not contribute to this stabilization. Importantly, we demonstrate that stabilizing p38 MAPK does not restore TNF biosynthesis. TNF biosynthesis is only restored with MK2 catalytic activity. We further show that, in MK2-deficient macrophages, formation of filopodia in response to extracellular stimuli is reduced. In addition, migration of MK2-deficient mouse embryonic fibroblasts (MEFs) and smooth muscle cells on fibronectin is dramatically reduced. Interestingly, reintroducing catalytic MK2 activity into MEFs alone is not sufficient to revert the migratory phenotype of these cells. In addition to catalytic activity, the proline-rich N-terminal region is necessary for rescuing the migratory phenotype. These data indicate that catalytic activity of MK2 is required for both cytokine production and cell migration. However, the proline-rich MK2 N terminus provides a distinct role restricted to cell migration.

=> d his

(FILE 'HOME' ENTERED AT 10:23:14 ON 19 NOV 2007)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 10:23:43 ON 19 NOV 2007

L1 3366 S "MAPKAP KINASE 2" OR MK2
L2 6 S SHC AND L1
L3 3 DUP REM L2 (3 DUPLICATES REMOVED)
L4 1 S L1 AND (YEAST (3W)ASSAY)
L5 919 S L1 AND (MODULATOR? OR INHIBITOR? OR ACTIVATOR?)
L6 1 S L5 AND (HYBRID ASSAY)
E YONNANI Y M/AU
E YANNONI Y/AU

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L7          48 S E3-E6
               E LIN L L/AU
L8         526 S E3
L9         570 S L7 OR L8
L10         23 S L1 AND L9
L11          7 DUP REM L10 (16 DUPLICATES REMOVED)
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	Document ID	Kind Codes	Source	Issue Date	Pages
1	US 20060094101 A1		US-PGPUB	20060504	52
2	US 20040219523 A1		US-PGPUB	20041104	286
3	US 20030027223 A1		US-PGPUB	20030206	48
4	US 7125660 B2		USPAT	20061024	276

	Title
1	Mk2 interacting proteins
2	Nucleic acid sensor molecules and methods of using same
3	Specimen-linked G protein coupled receptor database
4	Nucleic acid sensor molecules and methods of using same

	Document ID	Kind Codes	Source	Issue Date	Pages
1	US 20060094101 A1		US-PGPUB	20060504	52

	Title
1	Mk2 interacting proteins

	Document ID	Kind Codes	Source	Issue Date	Pages
1	US 20060094101 A1		US-PGPUB	20060504	52
2	US 20040219523 A1		US-PGPUB	20041104	286
3	US 20030027223 A1		US-PGPUB	20030206	48
4	US 7125660 B2		USPAT	20061024	276
5	US 6900043 B1		USPAT	20050531	61

	Title
1	Mk2 interacting proteins
2	Nucleic acid sensor molecules and methods of using same
3	Specimen-linked G protein coupled receptor database
4	Nucleic acid sensor molecules and methods of using same
5	Phosphatases which activate map kinase pathways

	Abstract	Current OR
1		435/194
2		435/6
3		435/7.21
4		435/4
5		435/196

	L #	Hits	Search Text
1	L1	1018	"mk2" or "mapkap kinase 2"
2	L2	2041	"shc"
3	L3	4	l1 same l2
4	L4	0	l1 same (yeast adj3 assay)
5	L5	1	l1 same (hybrid adj assay)
6	L6	120330	YANNONI LIN
7	L7	110	l1 and l6
8	L8	5	l7 and l2